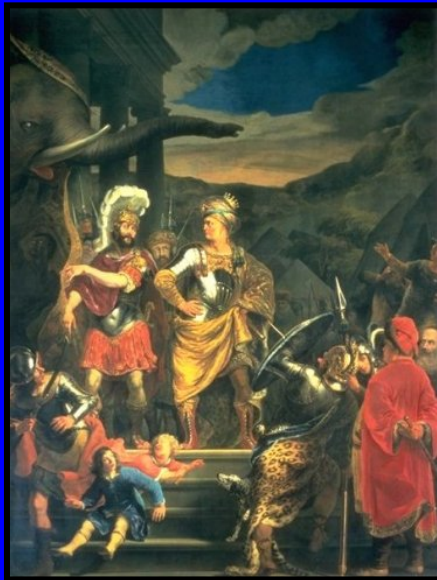


The Epidemiologic Conquest of Childhood Lead Poisoning

A Pyrrhic Victory

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Pyrrhic victory - A victory that is offset by staggering losses.

In 281, Pyrrhus, a Greek general, defeated the Romans in two battles, but suffered bitterly heavy losses.

The devastation led to his famous statement, "One more such victory and I am lost".

Evolution of Epidemiologic Studies

- First Generation (Case Series or Cross-Sectional)
- Second Generation (Prospective Cohorts)
- Third Generation (Representative Samples and RCTs)



Memorial to Dr A.J. Turner, President of the General Practitioners' Branch of the British Medical Association, 1908.



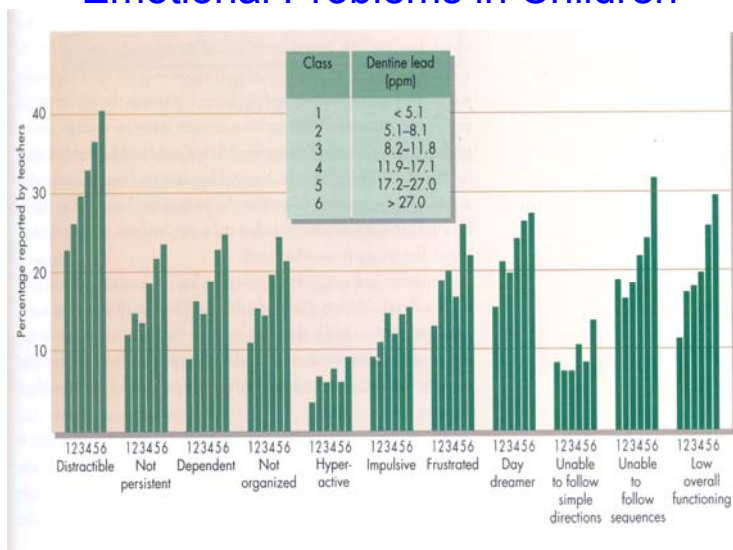
“Prevention is easy. Paint containing lead should never be employed ... where children, especially young children, are accustomed to play.”

A.J. Turner, 1908

Countries Banning Lead-based Paints

France	1909
Belgium	1909
Austria	1909
Tunisia	1922
Greece	1922
Czechoslovakia	1924
Great Britain	1926
Sweden	1926
Belgium	1926
Poland	1927
Spain	1931
Yugoslavia	1931
Cuba	1934

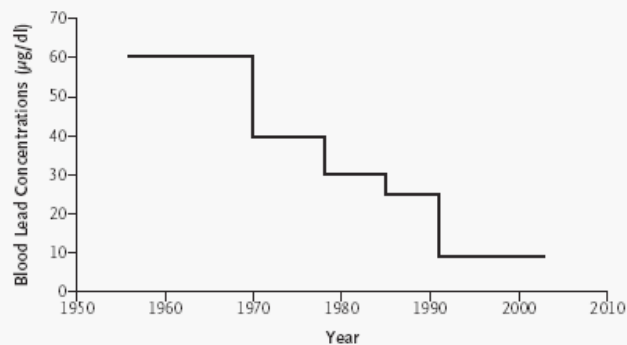
Lead-associated Behavioral and Emotional Problems in Children



Needleman HL, et al. N Engl J Med 1979;300:689-95.

Lead-associated IQ deficit linked with a blood lead increase from 10 μ g/dL to 20 μ g/dL

Study	Estimated Loss
Hawk (1986)	2.6
Hatzakis (1987)	2.7
Fulton (1987)	2.6
Yule (1981)	5.6
Bellinger (1992)	5.8
Dietrich (1992)	1.3
Baghurst (1992)	3.3
Silva (1988)	1.5

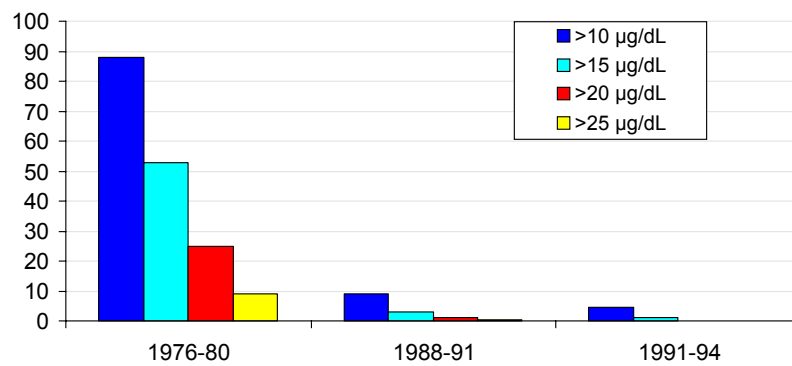


Blood Lead Concentrations Considered to Be Elevated by the Centers for Disease Control and Prevention.

To convert the values for blood lead concentrations to micromoles per liter, multiply by 0.0483. Data are from the Centers for Disease Control and Prevention, 1991.¹

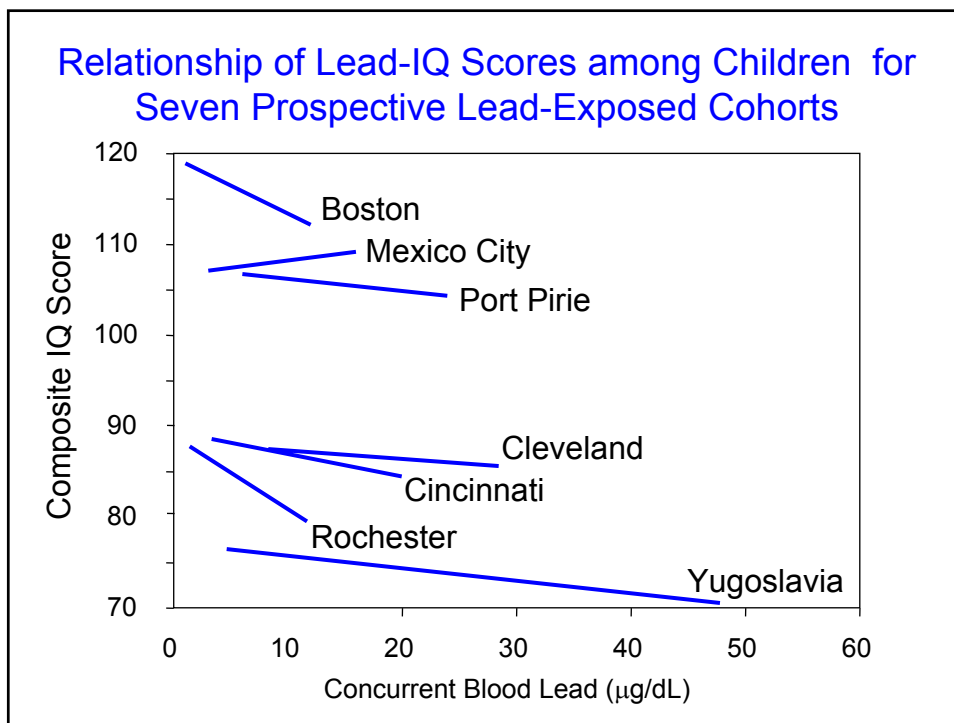
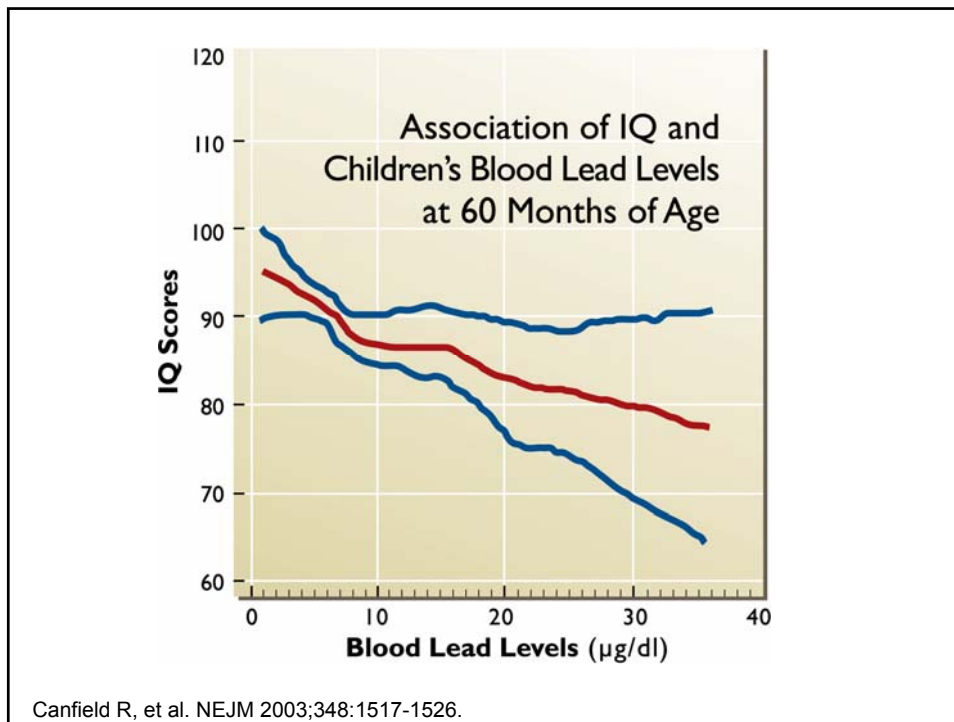
Binder S, Falk H. Strategic plan for the elimination of childhood lead poisoning. Atlanta: Centers for Disease Control, 1991.

Percent of U.S. Preschool Children Exceeding Selected Blood Lead Levels, NHANES II - III

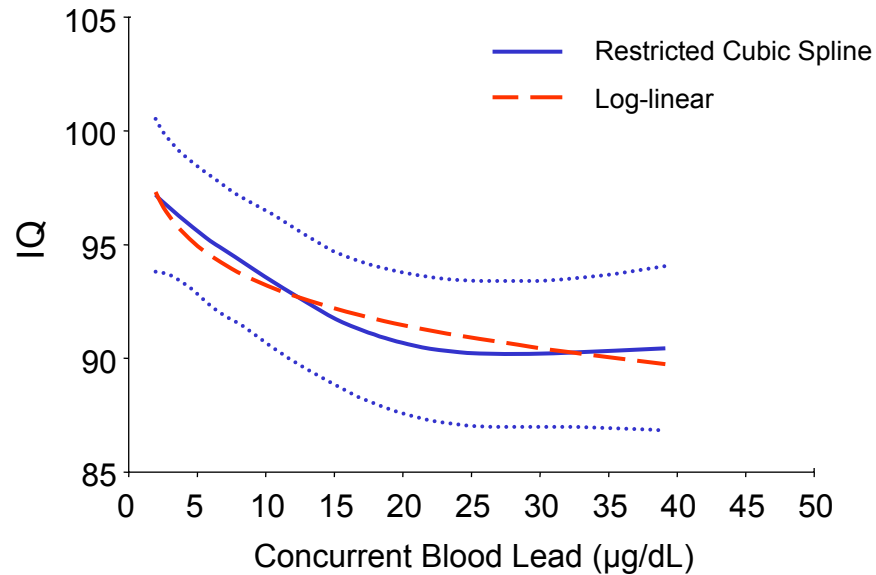


Pirkle JL, et al. Environ Health Perspect 1998;106:745-50.

Low-Level Lead Toxicity



Relationship of Concurrent Blood Lead Concentration with Children's Intellectual Function

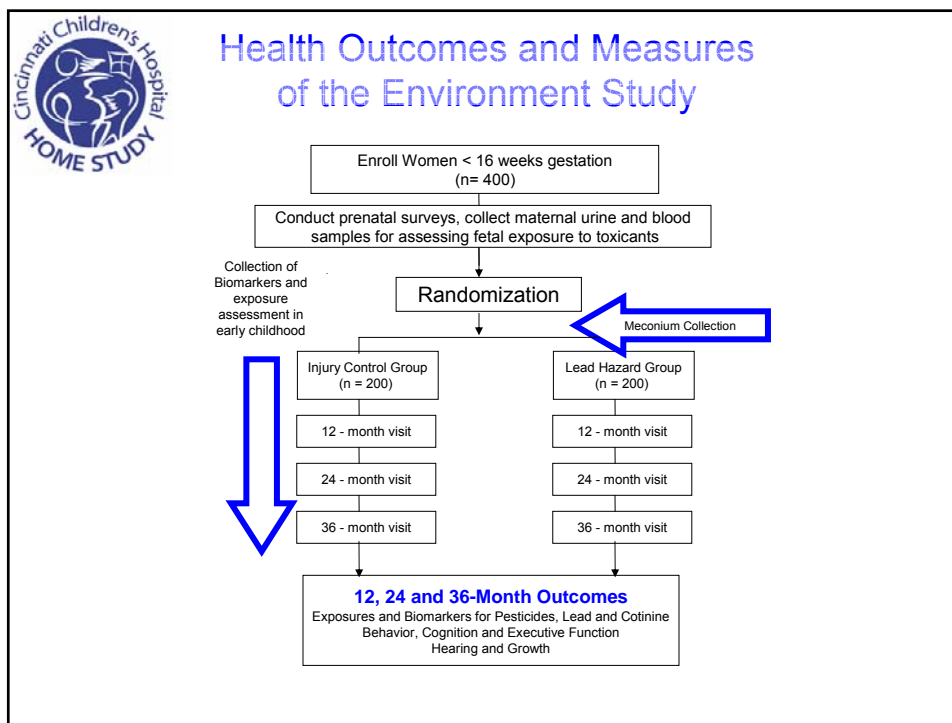


Estimated Lead-associated IQ Deficits by Concurrent Blood Lead Concentration

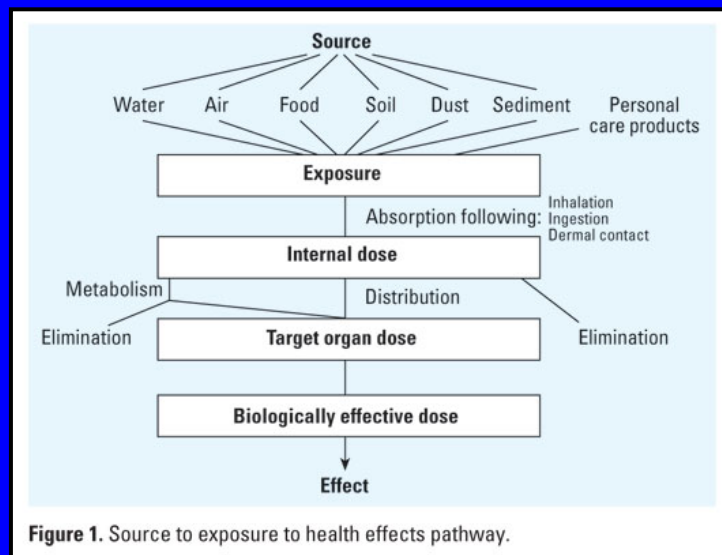
Range of Blood Lead	Estimated IQ Deficit (95% CI)
< 1 to 30 µg/dL	9.2 (5.7, 13.1)
<1 to 10 µg/dL	6.2 (3.8, 8.6)
10 to 20 µg/dL	1.9 (1.2, 2.6)
20 to 30 µg/dL	1.1 (0.7, 1.5)

Research Supporting Adverse Effects at Blood Lead Concentrations <10 µg/dL

- Fulton M, et al. Influence of blood lead on the ability and attainment of children in Edinburgh. *Lancet* 1987;1:1221-1226.
- Schwartz J. Low-level lead exposure and children's IQ: a meta-analysis and search for a threshold. *Environ Res* 1994;65:42-55.
- Walkowiak J, et al. Cognitive and sensorimotor functions in 6-year old children in relation to lead and mercury levels. *Neurotoxicol Teratol* 1998;20:511-521.
- Lanphear BP, et al. Cognitive deficits at blood lead levels <10 mg/dL in US children. *Public Health Reports* 2000;115:521-529.
- Wasserman G, et al. The Yugoslavia Prospective Lead Study: contributions of prenatal and postnatal lead exposure to early intelligence. *Neurotoxicol Teratol* 2000;22:811-818.
- Sood B, et al. Prenatal alcohol exposure and childhood behavior at age 6 to 7 years: I. dose-response effect. *Pediatrics*. 2001;108:E34.
- Chiodo LM, et al. Neurodevelopmental effects of postnatal lead exposure at very low levels. *Neurotoxicol Teratol* 2004;26:359-371.
- Kordas K, et al. Deficits in cognitive function and achievement in Mexican first-graders with low blood lead concentrations. *Environ Res* 2006;100:371-86.
- Tellez-Rojo M, et al. Longitudinal associations between blood lead concentrations lower than 10 mg/dL and neurobehavioral development in environmentally exposed children in Mexico City. *Pediatrics* 2006;118:e323-30.

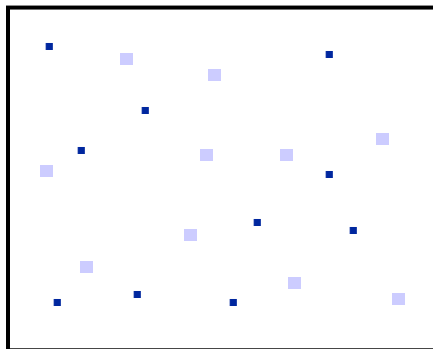
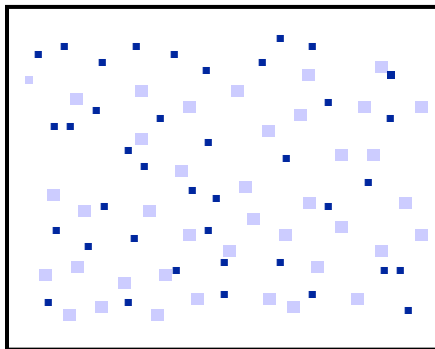


Evolution of Exposure Measurement

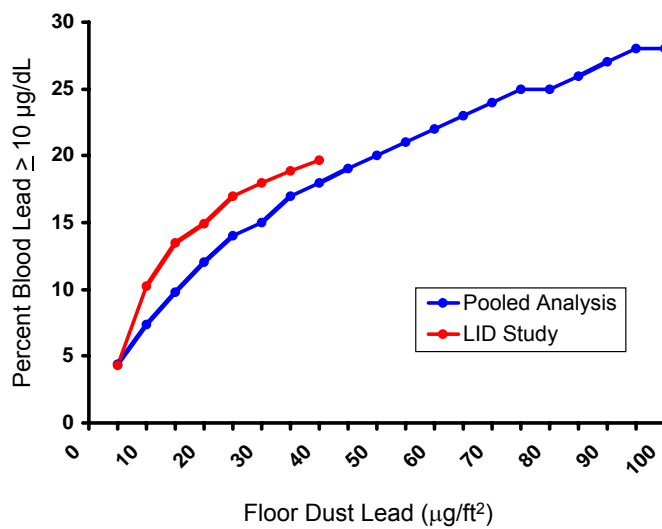


Needham L, et al. Environ Health Perspect 2005;113:1076-1082

Dust Lead Loading vs Dust Lead Concentration



Contribution of Lead-Contaminated Floor Dust to Children's Blood Lead



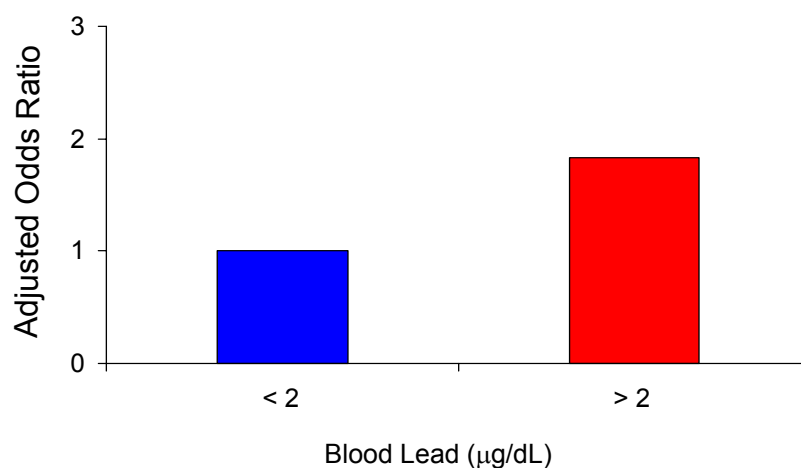
Lanphear BP, et al. Environmental Research 1998;79:51-68.

Biomarkers

Comparison of Biomarkers for Prenatal Lead Exposure

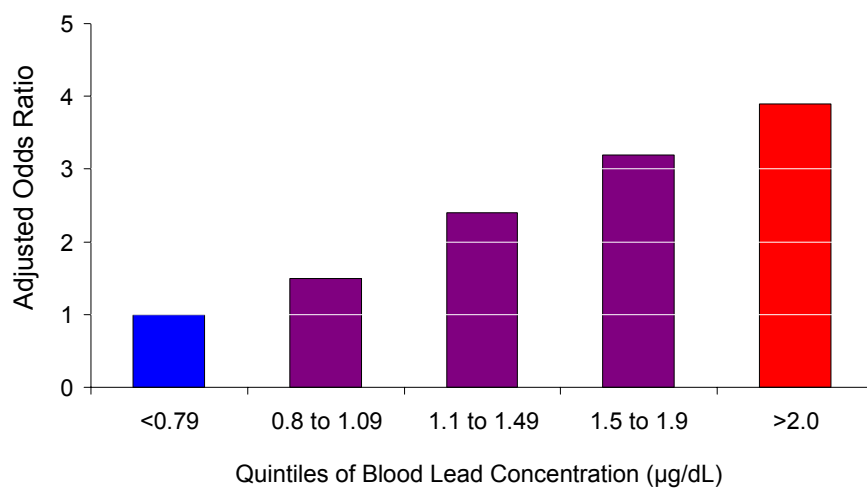
Sample	Blood	Plasma	Bone	Meconium
Validated	Yes	Yes	Yes	No
Invasive	Yes	Yes	No	No
Ease of Collection	+/-	+/-	+++	++
Detection Limit	+/-	+/-	+/-	++
Cumulative Measure	+/-	+/-	Yes	Yes
Window of Susceptibility	Yes	Yes	No	No
Cost	\$	\$\$	\$\$\$	\$\$

Risk of ADHD by Blood Lead Levels in US Children, NHANES 1999-2002



Braun J, et al. EHP 2006;114:500-505. Adjusted for child's age, sex, race and ethnicity, preschool attendance, serum ferritin, prenatal tobacco exposure and health insurance status.

Risk of ADHD by Blood Lead Levels in US Children, NHANES 1999-2002



Braun J, et al. EHP 2006;114:500-505. Adjusted for child's age, sex, race and ethnicity, preschool attendance, serum ferritin, prenatal tobacco exposure and health insurance status.

Plasma Lead Levels by MDI Scores at 24 Months of Age

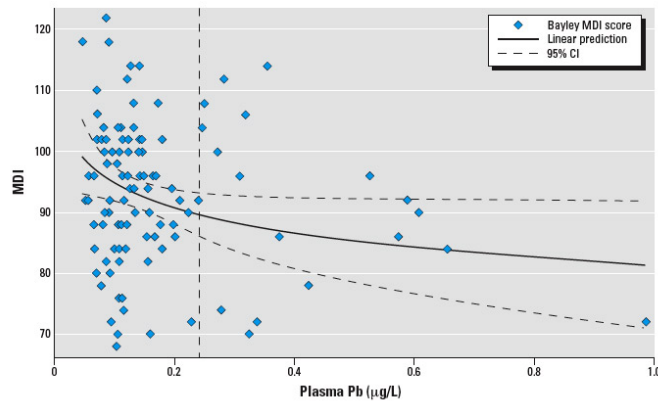
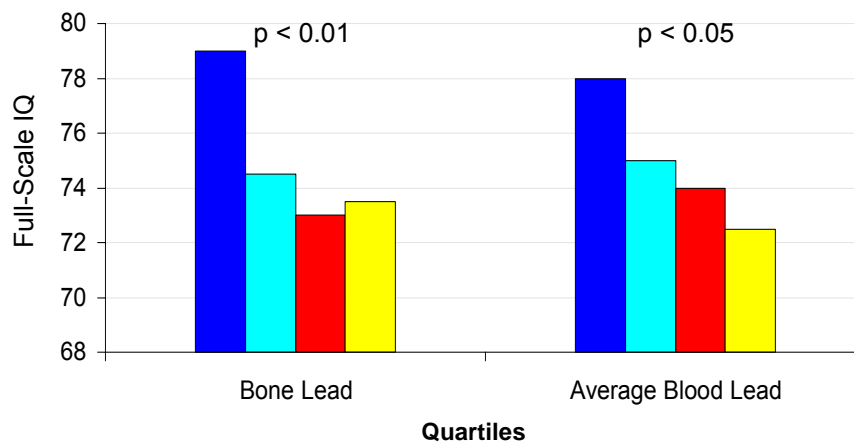


Figure 2. Plasma lead levels in the first trimester of pregnancy versus MDI scores at 24 months of age. CI, confidence interval. Curve indicates the best-fit model for the association between plasma lead levels and MDI scores, adjusting for plasma lead levels in the second and third trimesters, mother's age and IQ, child's blood lead levels at 24 months of age, sex and height-for-age Z-score. Vertical line marks average plasma lead concentration when whole blood lead equals 100 µg/L.

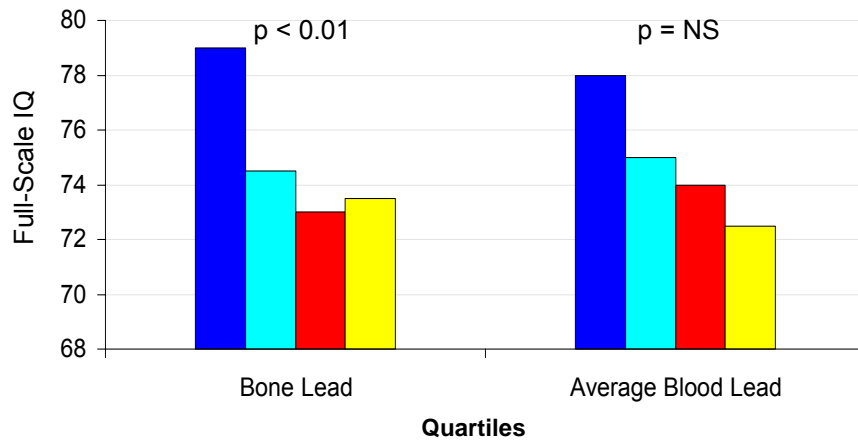
Hu H, et al. Environ Health Perspect 2006;114:1730–1735

Mean Adjusted Full-Scale IQ Scores by Quartiles for Tibial Bone Lead and Average Lifetime Blood Lead Levels



Wasserman GA, et al. Child Neuropsychol 2003;9:22-34.

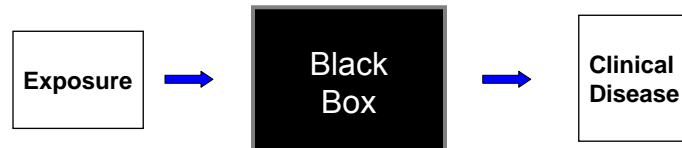
Mean Adjusted Full-Scale IQ Scores by Quartiles for Tibial Bone Lead and Average Lifetime Blood Lead Levels – Combined Analysis



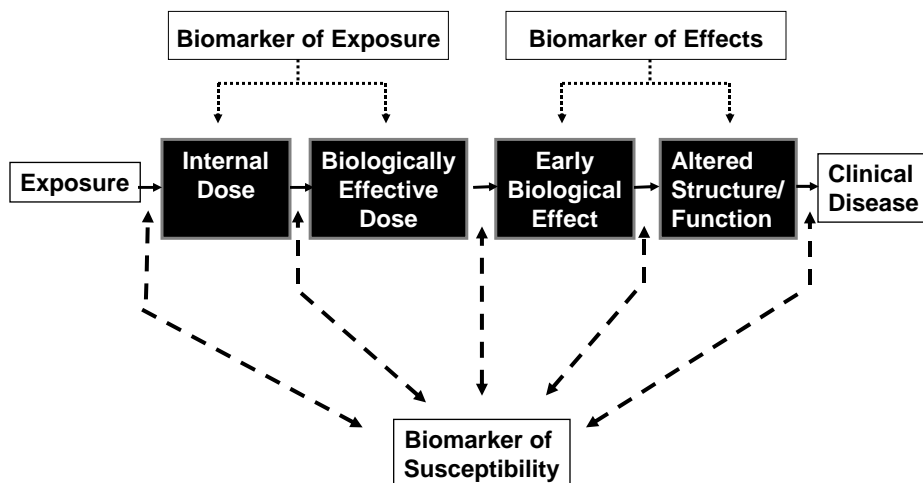
Wasserman GA, et al. Child Neuropsychol 2003;9:22-34.

Linkage of Lead Exposure with Lead-associated Disease and Disability

Traditional Epidemiology

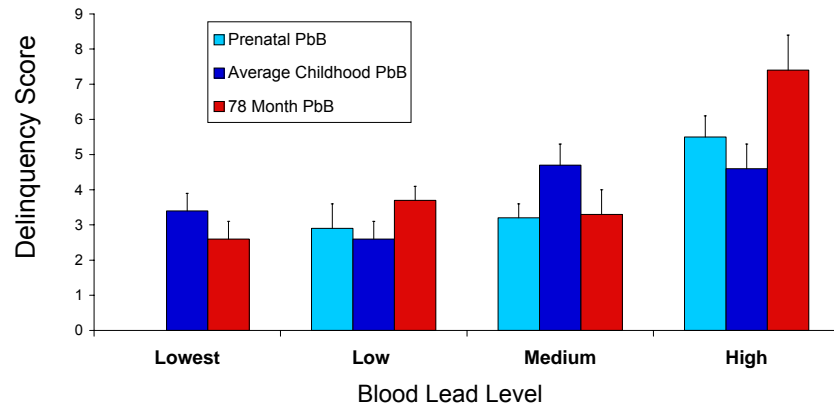


Linkage of Biomarkers of Exposure, Effect and Susceptibility with Disease or Disability



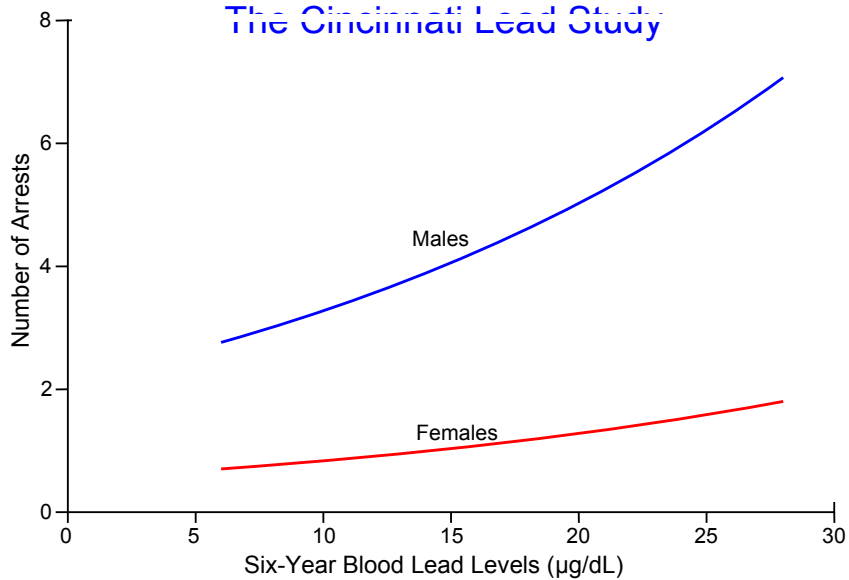
Perera FP, Weinstein IB. J Chronic Dis 1982;35:581-600.

Association of Blood Lead Levels and Delinquency in Adolescents



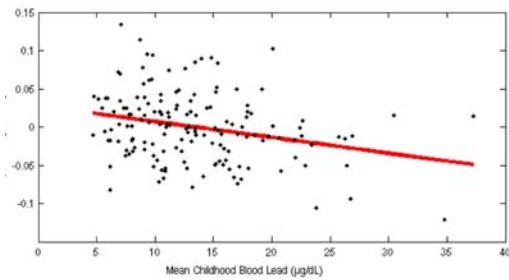
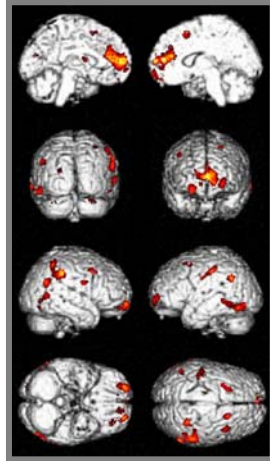
Dietrich KN, et al. Neurotox & Teratol 2001;23:511-518.

Number of Arrests by Childhood Lead Exposure: The Cincinnati Lead Study



* Accounting for birthweight, age, prenatal tobacco exposure, maternal age at delivery, maternal IQ, maternal arrest history, HOME Inventory.

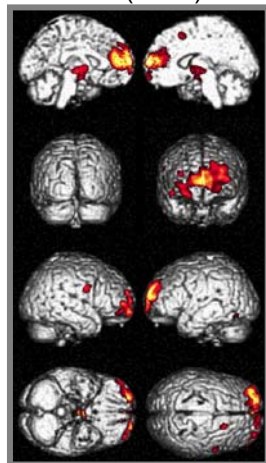
Grey Matter Loss by Childhood Lead Exposure (n=157)



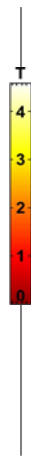
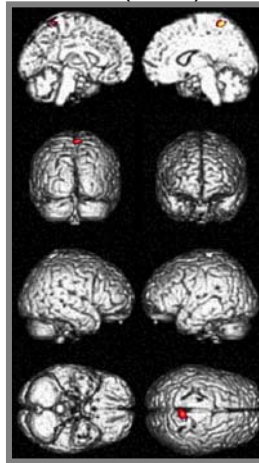
Adjusted for child's age, birth weight. Sex, gestational age, prenatal tobacco, prenatal alcohol, prenatal marijuana, total intracranial volume, SES and HOME Inventory did not alter results (Cecil K, Dietrich KN, et al. in preparation.)

Grey Matter Loss Associated with Childhood Lead Exposure by Sex

Males (n=83)

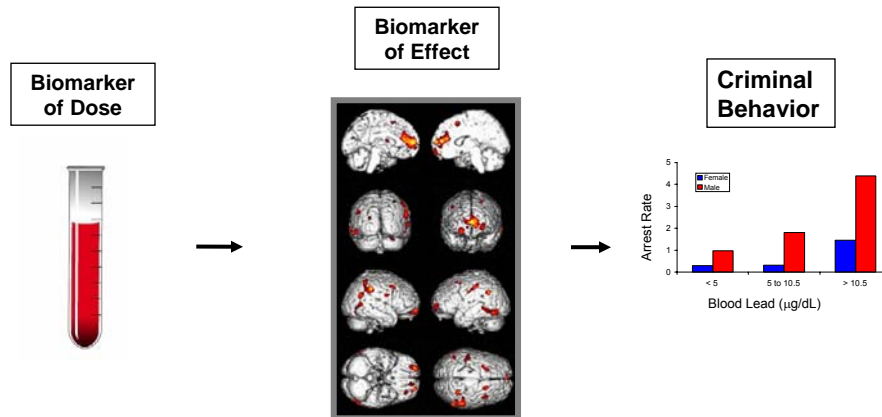


Females (n=74)



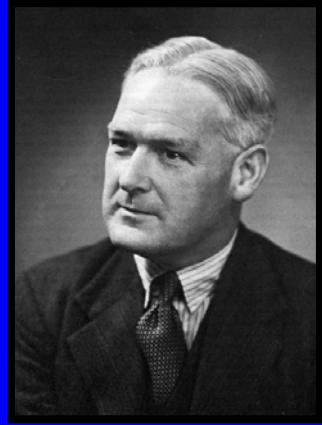
Adjusted for child's age, birth weight. Sex, gestational age, prenatal tobacco, prenatal alcohol, prenatal marijuana, total intracranial volume, SES and HOME Inventory did not alter results (Cecil K, Dietrich KN, et al. in preparation.)

Linking Putative Biomarkers of Lead Exposure and Effect with Criminal Behavior



Conclusions

- Expand research and validation for environmental exposure and biomarkers of internal dose
- RFA to target priorities vs reliance on investigator-initiated proposals (e.g., Children's Centers)
- Lengthen funding cycle for cohort studies
- Ensure National Children's Study is funded
- Expand NHANES to include exposure assessment and relevant measures of disease and disability
- Require pre-market DNT testing to ensure products are safe before dissemination in the environment



"All scientific work is incomplete – whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time."

Austin Bradford Hill

Hill AB. Proc Royal Soc Med 1965;58:295-300.